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Use of (2-hydroxyphenyl) alcohols and cosmetic or therapeutic formulations containing these compounds

The invention concerns the use of compounds from the group of (2-hydroxyphenyl) alcohols and its derivatives for the lightening of skin and/or hair and cosmetic or therapeutic formulations containing the compounds.

Skin-lightening active ingredients intervene in one form or another in melanin metabolism or catabolism. The melanin pigments, which are normally brown to black in colour, are formed in the melanocytes of the skin, transferred to the keratinocytes and give the skin or hair its colour. In mammals, the brown-black eumelanins are primarily formed from hydroxy-substituted aromatic amino acids such as L-tyrosine and L-DOPA, the yellow to red pheomelanins additionally from sulfur-containing molecules (*Cosmetics & Toiletries* **1996**, *111* (5), 43-51). Starting from L-tyrosine, L-3,4-dihydroxyphenylalanine (L-DOPA) is formed by the copper-containing key enzyme tyrosinase and is in turn converted by tyrosinase to dopachrome. By a series of steps catalysed by various enzymes, the latter is oxidised to form melanin.

Skin-lightening agents are used for various reasons: if for some reason the melanin-forming melanocytes in human skin are not evenly distributed, pigment spots occur which are either lighter or darker than the surrounding skin area. To overcome this problem, skin and hair lightening agents are sold which at least partially help to balance out such pigment spots. In addition, many people have a need to lighten their naturally dark skin colour or to prevent skin pigmentation. This requires very safe and effective skin and hair lightening agents. Many skin and hair lightening agents contain more or less strong tyrosinase inhibitors. This is only one possible route towards skin and hair lightening, however.

Furthermore, UV-absorbing substances are also used to protect against the increase in skin pigmentation caused by UV light. This is a purely physically induced effect, however, and must be distinguished from the biological action of skin-lightening agents on cellular melanin formation, which can also be detected in the absence of UV light. Moreover, UV absorbers bring about no true lightening of the skin but merely inhibit the increase in skin pigmentation caused by UV light.

Hydroquinone, hydroquinone derivatives such as e.g. arbutin, vitamin C, derivatives of ascorbic acid such as e.g. ascorbyl palmitate, kojic acid and derivatives of kojic acid such as e.g. kojic acid dipalmitate, are used in particular in commercial cosmetic or therapeutic skin and hair lightening formulations.

One of the most commonly used skin and hair lighteners is hydroquinone. However, this compound has a cytotoxic effect on melanocytes and is irritating to the skin. For that reason such preparations are no longer authorised for cosmetic applications in Europe, Japan and South Africa, for example. In addition, hydroquinone is very sensitive to oxidation and can be stabilised only with difficulty in cosmetic formulations.

Arbutin is a hydroquinone glucoside, which hydrolyses in situ to form hydroquinone and is therefore just as questionable in toxicological terms as hydroquinone.

Vitamin C and ascorbic acid derivatives have only an inadequate effect on the skin. Furthermore, they do not act directly as tyrosinase inhibitors but instead reduce the coloured intermediate stages of melanin biosynthesis.

Kojic acid (5-hydroxy-2-hydroxymethyl-4-pyranone) is a tyrosinase inhibitor which inhibits its catalytic action by chelating the copper atoms in the enzyme; it is used in commercial skin and hair lightening agents but has a high sensitising potential and causes contact allergies.

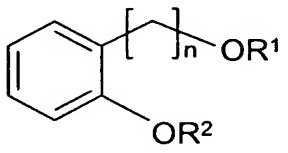
Salicin is widely used in cosmetics as an active agent against wrinkles, old, dry and rough skin and as a protection against inflammations and to promote wound healing.

In JP 2002275060 A2 salicylic acid and salicylic alcohol derivatives are described as active ingredients which stimulate skin browning.

Funayama et al. (Seibutsu Kogaku Kaishi (1997), 75(5), 333-337) have examined the inhibition of melanogenesis by various polyphenol glucosides on B16 mouse melanoma cells, including 2-hydroxybenzyl alcohol-α-D-glucoside (α-salicin). No inhibition of melanogenesis in B16 cells was found for this last compound, however.

The object of the present invention was to remedy the disadvantages of the prior art and in particular to provide highly effective skin lighteners which preferably inhibit tyrosinase or other cellular mechanisms of pigmentation.

In accordance with a first aspect of the present invention, the specified object is achieved through the use of a compound having the formula (I)

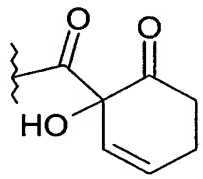


(I)

wherein:

n = 1-10,

R^1 is selected from the group comprising: H, branched or unbranched C_1-C_{14} alkyl, branched or unbranched C_2-C_{14} alkenyl, branched or unbranched C_2-C_{14} alkynyl, substituted or unsubstituted aryl alkyl, cyclohexyl, cyclopentyl, substituted or unsubstituted phenyl, substituted or unsubstituted monosaccharide, SO_3H, SO_3Na,



$(CH_2)_{1\text{-}10}OH$, COR, SiRR'R", PO_3HNa, PO_3Na_2 and ,

wherein R, R', R" are mutually independently selected from the group comprising: H, C_1-C_{14} alkyl, C_2-C_{14} alkenyl, C_2-C_{14} alkynyl, cyclohexyl, cyclopentyl, substituted or unsubstituted phenyl and heterocyclic ring,

and

R^2 is an enzymatically cleavable substituent or is selected from the group comprising: H, branched or unbranched C_1-C_{14} alkyl, branched or unbranched C_2-C_{14} alkenyl, branched or unbranched C_2-C_{14} alkynyl, cyclohexyl, cyclopentyl, substituted and unsubstituted phenyl or substituted or unsubstituted aryl alkyl

for the lightening of skin and/or hair.

The compounds having formula (I) include their stereoisomers and tautomers and any mixtures of these isomers. The compounds having formula (I) also include all associated salts, in particular alkali and alkaline-earth salts.

Surprisingly it was found in our own investigations that the compounds having formula (I) for use according to the invention inhibit the pigmentation of melanocytes particularly efficiently. In particular, many of the (2-hydroxyphenyl) alcohols according to the invention are substantially more

effective than kojic acid. They can therefore be used outstandingly well as active ingredients in cosmetic (including dermatological) and therapeutic skin and hair lightening agents.

Within the group of compounds having formula (I), which can be used according to the invention for the lightening of skin and hair, compounds are preferred wherein

R^2 is an enzymatically cleavable substituent from the group comprising SO_3H, SO_3Na, $(CH_2)_{1-10}OH$, COR, PO_3HNa and PO_3Na_2, wherein R, R' are mutually independently selected from the group comprising: H, C_1-C_{14} alkyl, C_2-C_{14} alkenyl, C_2-C_{14} alkynyl, cyclohexyl, cyclopentyl, substituted or unsubstituted phenyl and heterocyclic ring,

or

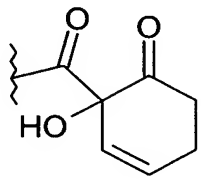
R^2 is an enzymatically cleavable, substituted or unsubstituted monosaccharide from the group comprising glucose, mannose or galactose.

The last-named monosaccharides are preferably in the form of a pyranose. Substituted monosaccharides include in particular 6'-O-acetyl pyranoses, 6'-O-benzoyl pyranoses, 2'-O-acetyl pyranoses and 2'-O-benzoyl pyranoses.

Moreover, within the group of compounds having formula (I) – particularly in the presence of a substituent R^2 which is enzymatically cleavable in the manner previously described – compounds are preferred wherein:

n = 1-4,

R^1 is selected from the group comprising: H, branched or unbranched C_1-C_{14} alkyl, branched or unbranched C_2-C_{14} alkenyl, branched or unbranched C_2-C_{14} alkynyl, substituted or unsubstituted aryl alkyl, substituted or unsubstituted

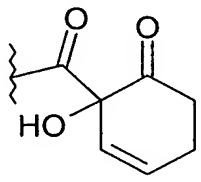
phenyl, substituted or unsubstituted monosaccharide, $(CH_2)_{1-10}OH$, COR, SR, PO_3RR' and 

,

wherein R, R' are mutually independently selected from the group comprising: H and C_1-C_{14} alkyl.

Also preferred are compounds having formula (I) wherein

n = 1-4,

R^1 is selected from the group comprising: H, branched or unbranched C_1-C_{14} alkyl, branched and unbranched C_2-C_{14} alkenyl, branched or unbranched C_2-C_{14} alkynyl, substituted or unsubstituted aryl alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted monosaccharide, $(CH_2)_{1-10}OH$, COR, SR, PO_3RR' and 

, wherein R, R' are mutually independently selected from the group comprising: H and C_1-C_{14} alkyl,

and

R^2 is selected from the group comprising: H, branched or unbranched C_1-C_{14} alkyl, branched or unbranched C_2-C_{14} alkenyl, branched or unbranched C_2-C_{14} alkynyl and substituted or unsubstituted phenyl.

Alternatively or in addition to the aforementioned preferred choices of compounds, within the group of compounds having formula (I) which can be used according to the invention for lightening of skin and hair, compounds are preferred wherein n = 2 – 10, in particular n = 2 – 4.

The specified object is achieved in particular by the use of saligenin (2-hydroxybenzyl alcohol), fragilin (6'-O-acetyl salicin), populin (6'-O-benzoyl salicin), tremuloidin (2'-benzoyl salicin), salicortin, 2-O-acetyl salicortin or tremulacin (2-O-benzoyl salicortin) for lightening of skin and/or hair. Most particularly preferred within the meaning of the invention is salicin ((hydroxymethyl)phenyl-β-D-glucopyranoside).

A second aspect of the invention concerns cosmetic or therapeutic formulations, in particular topical cosmetic formulations, which contain an amount having a lightening effect on skin and/or hair of one or more compounds having formula (I). All above statements regarding the selection of substituents naturally also apply in this respect.

The cosmetic or therapeutic formulations according to the invention are produced by conventional processes known per se, such that one or more of the (2-hydroxyphenyl) alcohols used according to the invention are incorporated into cosmetic or dermatological formulations which have a conventional composition and which in addition to the skin and hair lightening effect can also be used for the treatment, care and cleansing of the skin or hair and as makeup products in decorative cosmetics.

The present invention accordingly also concerns (in particular) topical cosmetic or therapeutic formulations, in particular cosmetic (including dermatological) skin and hair lightening agents, which comprise the (2-hydroxyphenyl) alcohols for use according to the invention in an effective amount, in addition to other otherwise conventional compositional constituents. Formulations according to the invention preferably contain 0.01 wt.% to 30 wt.%, preferably 0.01 to 20 wt.%, but in particular 0.01 wt.% to 5 wt.%, based on the total weight of the formulation, of the (2-hydroxyphenyl) alcohols for use according to the invention and can take the form of "water in oil", "oil in water, "water in oil in water", "oil in water in oil" emulsions, PIT emulsions, Pickering emulsions, emulsions having a low oil content, microemulsions, gels, solutions, e.g. in oils, alcohols or silicone oils, sticks, soaps, aerosols, sprays or foams or impregnating solutions for cosmetic wipes. It is also advantageous to administer the (2-hydroxyphenyl) alcohols in encapsulated form, e.g. in gelatine, wax materials, liposomes or cellulose

capsules. Other conventional cosmetic auxiliary substances and additives can be included in quantities of 5 to 99 wt.%, preferably 10 to 80 wt.%, based on the total weight of the formulation. The formulations can also contain water in a quantity of up to 99.99 wt.%, preferably 5 to 80 wt.%, based on the total weight of the formulation.

No mention is made in the prior art of a depigmenting action of compounds having formula (I) or of their use in skin and hair lightening agents.

The (2-hydroxyphenyl) alcohols having formula (I) according to the invention can be extracted for example from willow bark (Salix purpurea or Salix daphinoides) and purified by chromatography or two-phase extraction or produced enzymatically from 2-hydroxybenzyl alcohol by means of hydrolases such as e.g. glycosidases or lipases.

The cosmetic or therapeutic (especially topical) formulations according to the invention, in particular skin and hair lightening agents, can contain cosmetic auxiliary substances and additives such as are conventionally used in such preparations, e.g. sunscreens, preservatives, bactericides, fungicides, virucides, cooling agents, insect repellents (e.g. DEET, IR 3225, Dragorepel), plant extracts, anti-inflammatory agents, substances to accelerate wound healing (e.g. chitin or chitosan and derivatives thereof), film-forming substances (e.g. polyvinyl pyrrolidones or chitosan or derivatives thereof), conventional antioxidants, vitamins (e.g. vitamin C and derivatives, tocopherols and derivatives, vitamin A and derivatives), 2-hydroxycarboxylic acids (e.g. citric acid, malic acid, L-, D- or dl-lactic acid), skin colouring agents (e.g. walnut extracts or dihydroxyacetone), skin care agents (e.g. cholesterol, ceramides, pseudoceramides), softening, moisturising and/or moisture-retaining substances (e.g. glycerol or urea), fats, oils, saturated fatty acids, monounsaturated or polyunsaturated fatty acids, α-hydroxy acids, polyhydroxy fatty acids or derivatives thereof (e.g. linoleic acid, α-linolenic acid, γ-linolenic acid or arachidonic acid and the natural or synthetic esters thereof), waxes or other conventional constituents of a cosmetic or dermatological formulation such as alcohols, polyols, polymers, foam stabilisers, electrolytes, organic solvents, silicone derivatives or chelating agents (e.g. ethylene diamine

tetraacetic acid and derivatives), anti-dandruff agents (e.g. climbazole, ketoconazole, piroctone olamine, zinc pyrithione), hair care products, perfumes, substances to prevent foaming, dyes, pigments having a colouring action, thickeners, surface-active substances, emulsifiers, plant parts and plant extracts (e.g. arnica, aloe, beard lichen, ivy, stinging nettle, ginseng, henna, camomile, marigold, rosemary, sage, horsetail or thyme), animal extracts such as e.g. royal jelly, propolis, proteins, protein hydrolysates, yeast extracts, hop and wheat extracts, peptides or thymus extracts.

The amounts of cosmetic or dermatological auxiliary agents and additives and perfume to be used in each case can easily be determined by the person skilled in the art by simple trial and error, depending on the nature of the particular product.

The amount of the aforementioned examples of active ingredients for skin and hair lightening (one or more compounds) in the cosmetic and dermatological preparations according to the invention can be 0.01 to 30 wt.%, preferably 0.01 to 20 wt.%, particularly preferably 0.01 to 5 wt.%, based on the total weight of the preparation.

The formulations according to the invention can preferably also contain other active ingredients which stimulate skin and hair tinting or lightening by chemical or natural means. A more rapid action based on synergistic effects is achieved in this way. Particularly preferred here are substrates or substrate analogues of tyrosinase such as L-tyrosine, L-DOPA or L-dihydroxyphenylalanine, stimulators of tyrosinase activity or expression such as theophylline, caffeine, proopiomelanocortin peptides such as ACTH, alpha-MSH, peptide analogues thereof and other substances which bind to the melanocortin receptor, purines, pyrimidines, folic acid, phenylalanine derivatives such as e.g. undecylenoyl phenylalanine, diacylglycerols, aliphatic or cyclic diols, psoralens, prostaglandins and analogues thereof, activators of adenylate cyclase and compounds which activate the transfer of melanosomes into keratinocytes such as serine proteases or agonists of the PAR-2 receptor, extracts of plants and plant parts of the chrysanthemum species, walnut extracts, erythrulose and dihydroxyacetone.

The formulations according to the invention can also additionally contain UV-A and/or UV-B filter substances such as e.g. Neo Heliopans®, however, wherein the total amount of filter substances can be 0.1 to 30 wt.%, particularly preferably 0.2 to 10 wt.%, in particular 0.5 to 5 wt.%, based on the total weight of the preparations, wherein for example sunscreens for skin and hair are obtained.

Suitable light stabilisers are, for example, organic UV absorbers from the class comprising 4-aminobenzoic acid and derivatives, salicylic acid derivatives, benzophenone derivatives, dibenzoylmethane derivatives, diphenyl acrylates, 3-imidazol-4-yl acrylic acid and esters thereof, benzofuran derivatives, benzylidene malonate derivatives, polymeric UV absorbers (containing one or more organosilicon radicals), cinnamic acid derivatives, camphor derivatives, trianilino-s-triazine derivatives, 2-hydroxyphenylbenzotriazole derivatives, phenylbenzimidazole sulfonic acid derivatives and salts thereof, anthranilic acid menthyl esters, benzotriazole derivatives, indole derivatives.

The following list of UV absorbers which can be used within the meaning of the present invention is naturally not intended to be limiting.

4-Aminobenzoic acid, 4-aminobenzoic acid ethyl ester, 4-dimethylaminobenzoic acid-2-ethylhexyl ester, 4-aminobenzoic acid glycerol ester, salicylic acid homomenthyl ester (homosalate), salicylic acid-2-ethylhexyl ester, triethanolamine salicylate, 4-isopropylbenzyl salicylate, anthranilic acid menthyl ester, diisopropyl cinnamic acid ethyl ester, p-methoxycinnamic acid-2-ethylhexyl ester, diisopropyl cinnamic acid methyl ester, p-methoxycinnamic acid isoamyl ester, p-methoxycinnamic acid diethanolamine salt, p-methoxycinnamic acid isopropyl ester, 2-ethylhexyl-2-cyano-3,3-diphenyl acrylate, ethyl-2-cyano-3,3'-diphenyl acrylate, 2-phenylbenzimidazole-5-sulfonic acid and salts thereof, 3-(4'-trimethylammonium)benzylidene bornan-2-one methyl sulfate, terephthalylidene dibornane sulfonic acid and salts, 4-t-butyl-4'-methoxydibenzoyl methane, ß-imidazole-4(5)-acrylic acid (urocanic acid), 2-hydroxy-4-methoxybenzophenone, 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid, dihydroxy-4-methoxybenzophenone, 2,4-dihydroxybenzophenone, tetrahydroxybenzophenone, 2,2'-dihydroxy-4,4'-

dimethoxybenzophenone, 2-hydroxy-4-n-octoxybenzophenone, 2-hydroxy-4-methoxy-4'-methylbenzophenone, 3-(4'-sulfo)benzylidene bornan-2-one and salts thereof, 3-(4'-methylbenzylidene) camphor, 3-benzylidene camphor, 3,3'-(1,4-phenylene dimethine)-bis-(7,7-dimethyl-2-oxo-bicyclo-[2.2.1]heptane-1-methane sulfonic acid and salts thereof, 4-isopropyl dibenzoylmethane, 2,4,6-trianilino-(p-carbo-2'-ethylhexyl-1'-oxy)-1,3,5-triazine, phenylene-1,4-bis-(2-benzimidazyl)-3,3'-5,5'-tetrasulfonic acid and salts thereof, especially the corresponding sodium, potassium or triethanolammonium salts, in particular the disodium salt, 2,2'-(1,4-phenylene)-bis-(1H-benzimidazole-4,6-disulfonic acid), monosodium salt, N-[(2 and 4)-[2-(oxoborn-3-ylidene)methyl]benzyl] acrylamide polymer, phenol, 2-(2H-benzotriazol-2-yl)-4-methyl-6-(2-methyl-3-(1,3,3,3-tetramethyl-1-(trimethylsilyl)oxy)disiloxyanyl) propyl), 4,4'-[(6-[4-(1,1-dimethyl) aminocarbonyl) phenylamino]-1,3,5-triazine-2,4-diyl)diimino] bis-(benzoic acid-2-ethylhexyl ester), 2,2'-methylene bis-(6-(2H-benzotriazol-2-yl)-4-1,1,3,3-tetramethylbutyl) phenol), 2,4-bis-[4-(2-ethylhexyloxy)-2-hydroxyphenyl]-1,3,5-triazine, benzylidene malonate polysiloxane, glyceryl ethylhexanoate dimethoxycinnamate, disodium-2,2'-dihydroxy-4,4'-dimethoxy-5,5'-disulfobenzophenone, dipropylene glycol salicylate, sodium hydroxymethoxybenzophenone sulfonate, 4,4',4-(1,3,5-triazine-2,4,6-triyltriimino)-tris-benzoic acid tris(2-ethylhexyl ester), 2,4-bis-[{(4-(2-ethylhexyloxy)-2-hydroxy}phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine, 2,4-bis-[{(4-(3-sulfonato)-2-hydroxypropyloxy)-2-hydroxy}phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine sodium salt, 2,4-bis-[{(3-(2-propyloxy)-2-hydroxypropyloxy)-2-hydroxy}phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine, 2,4-bis-[{4-(2-ethylhexyloxy)-2-hydroxy}phenyl]-6-[4-(2-methoxyethyl carbonyl) phenylamino]-1,3,5-triazine, 2,4-bis-[{4-(3-(2-propyloxy)-2-hydroxypropyloxy)-2-hydroxy}phenyl]-6-[4-(2-ethylcarboxyl)phenylamino]-1,3,5-triazine, 2,4-bis-[{4-(2-ethylhexyloxy)-2-hydroxy}phenyl]-6-(1-methyl pyrrol-2-yl)-1,3,5-triazine, 2,4-bis-[{4-tris-(trimethylsiloxysilylpropyloxy)-2-hydroxy}phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine, 2,4-bis-[{4-(2"-methylpropenyloxy)-2-hydroxy}phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine, 2,4-bis-[{4-(1',1',1',3',5',5',5'-heptamethylsiloxy-2"-methylpropyloxy)-2-hydroxy}phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine, 2-(4-diethylamino-2-hydroxybenzoyl) benzoic acid hexyl ester.

Furthermore, particulate UV filters or inorganic pigments, which can optionally be hydrophobed, can be used, such as the oxides of titanium (TiO_2), zinc (ZnO), iron (Fe_2O_3), zirconium (ZrO_2), silicon (SiO_2), manganese (e.g. MnO), aluminium (Al_2O_3), cerium (e.g. Ce_2O_3) and/or mixtures.

The formulations according to the invention can also contain (additional) antioxidants or preservatives. All antioxidants which are suitable or commonly used for cosmetic and/or dermatological applications can be used as antioxidants or preservatives.

Antioxidants within the meaning of the invention are all substances which lower the amount of free radicals in cells and tissue. Antioxidants are advantageously chosen from the group comprising amino acids (e.g. glycine, histidine, tyrosine, tryptophane) and derivatives thereof, imidazoles (e.g. urocanic acid) and derivatives thereof, peptides such as D,L-carnosine, D-carnosine, L-carnosine and derivatives thereof (e.g. anserine), carotenoids, carotenes (e.g. α-carotene, β-carotene, lycopene) and derivatives thereof, lipoic acid and derivatives thereof (e.g. dihydrolipoic acid), aurothioglucose, propyl thiouracil and other thiols (e.g. thioredoxine, glutathione, cysteine, cystine, cystamine and glycosyl, N-acetyl, methyl, ethyl, propyl, amyl, butyl and lauryl, palmitoyl, oleyl, γ-linoleyl, cholesteryl, glyceryl and oligoglyceryl esters thereof) and salts thereof, dilauryl thiodipropionate, distearyl thiodipropionate, thiodipropionic acid and derivatives thereof (esters, ethers, peptides, lipids, nucleotides, nucleosides and salts) and sulfoximine compounds (e.g. buthionine sulfoximines, homocysteine sulfoximine, buthionine sulfones, penta-, hexa-, heptathionine sulfoximine) in very small tolerated doses (e.g. pmol to μmol/kg), also (metal) chelators (e.g. α-hydroxy fatty acids, palmitic acid, phytic acid, lactoferrin), α-hydroxy acids (e.g. citric acid, lactic acid, malic acid), humic acid, bile acid, bile extracts, tannins, bilirubin, biliverdin, EDTA, EGTA and derivatives thereof, unsaturated fatty acids and derivatives thereof (e.g. γ-linolenic acid, linoleic acid, oleic acid), folic acid and derivatives thereof, ubiquinone and ubiquinol and derivatives thereof, vitamin C and derivatives (e.g. ascorbyl palmitate, Mg ascorbyl phosphate, ascorbyl acetate), tocopherols and derivatives (e.g. vitamin E acetate), vitamin A and derivatives (vitamin A palmitate) and coniferyl

benzoate of benzoic resin, rutinic acid and derivatives thereof, ferulic acid and derivatives thereof, caffeic acid and derivatives thereof, sinapic acid and derivatives thereof, curcuminoids and derivatives thereof, retinoids, ursolic acid, levulinic acid, butyl hydroxytoluene, butyl hydroxyanisole, nordihydroguaiac acid, nordihydroguaiaretic acid, trihydroxybutyrophenone, uric acid and derivatives thereof, mannose and derivatives thereof, zinc and derivatives thereof (e.g. ZnO, $ZnSO_4$), selenium and derivatives thereof (e.g. selenium methionine), stilbenes and derivatives thereof (e.g. stilbene oxide, trans-stilbene oxide) and the derivatives (salts, esters, ethers, sugars, nucleotides, nucleosides, peptides and lipids) of these cited active ingredients that are suitable according to the invention. Natural extracts, e.g. from green tea, algae, grape seeds, wheat germ, Phyllantus emblica, rosemary; flavonoids, the glycosylated precursors thereof, quercetin, phenolic benzylamines.

Also suitable are coenzymes, such as e.g. coenzyme Q10, plastoquinone, menaquinone, ubiquinols 1-10, ubiquinones 1-10 or derivatives of these substances.

The amount of antioxidants (one or more compounds) in the formulations according to the invention is preferably 0.01 to 20 wt.%, particularly preferably 0.05 to 10 wt.%, in particular 0.2 to 5 wt.%, based on the total weight of the preparation.

If vitamin E and/or derivatives thereof are used as the antioxidant(s), it is advantageous to choose their concentrations from the range from 0.001 to 10 wt.%, based on the total weight of the formulation.

If vitamin A or vitamin A derivatives or carotenes or derivatives thereof are used as the antioxidant(s), it is advantageous to choose their concentrations from the range from 0.001 to 10 wt.%, based on the total weight of the formulation.

The use of anti-irritants in the formulations according to the invention can also be advantageous. Anti-irritants in this connection can be all anti-inflammatory active ingredients or active ingredients to relieve reddening and itching which

are suitable for or commonly used in cosmetic and/or dermatological applications. All substances which reduce the amount of cytokines, interleukins, prostaglandins and/or leukotrienes in cells and tissue are preferred.

Steroidal anti-inflammatory substances of the corticosteroid type, such as e.g. hydrocortisone, dexamethasone, dexamethasone phosphate, methyl prednisolone or cortisone, are advantageously used as anti-inflammatory active ingredients or active ingredients relieving reddening and itching, the list of which can be extended by the addition of other steroidal anti-inflammatories. Non-steroidal anti-inflammatories can also be used. Examples which can be cited here are oxicams such as piroxicam or tenoxicam; salicylates such as aspirin, disalcid, solprin or fendosal; acetic acid derivatives such as diclofenac, fenclofenac, indomethacin, sulindac, tolmetin or clindanac; fenamates such as mefenamic, meclofenamic, flufenamic or niflumic; propionic acid derivatives such as ibuprofen, naproxen, benoxaprofen or pyrazoles such as phenylbutazone, oxyphenylbutazone, febrazone or azapropazone. Alternatively, natural anti-inflammatory substances or substances to relieve reddening and itching can be used. Plant extracts, special highly active plant extract fractions and highly pure active substances isolated from plant extracts can be used. Particularly preferred are extracts, fractions and active substances from camomile, aloe vera, commiphora species, rubia species, echinacea species, willow, willowherb, oats, black and green tea, gingko, coffee, pepper, blackcurrant, tomato, vanilla, almonds, as well as pure substances such as inter alia bisabolol, apigenin-7-glucoside, boswellic acid, phytosterols, glycyrrhizinic acid, glabridin or licochalcone A.

The amount of anti-irritants (one or more compounds) in the formulations according to the invention is preferably 0.01 to 20 wt.%, particularly preferably 0.03 to 10 wt.%, in particular 0.05 to 5 wt.%, based on the total weight of the preparation.

The formulations according to the invention (in particular topical cosmetic formulations) can also contain moisture regulators. The following substances, for example, can be used as moisture regulators (moisturisers): sodium lactate, urea, alcohols, sorbitol, glycerol, propylene glycol, collagen, elastin or

hyaluronic acid, diacyl adipates, petroleum jelly, ectoine, urocanic acid, lecithin, pantheol, phytanetriol, lycopene, algal extracts, ceramides, cholesterol, glycolipids, chitosan, chondroitin sulfate, polyamino acids and sugars, lanolin, lanolin esters, amino acids, alpha-hydroxy acids (e.g. citric acid, lactic acid, malic acid) and derivatives thereof, sugars (e.g. inositol), alpha-hydroxy fatty acids, phytosterols, triterpene acids such as betulinic acid or ursolic acid, algal extracts.

The lipid phase in the formulations according to the invention (in particular topical cosmetic formulations) can advantageously be selected from the following groups of substances: mineral oils (advantageously paraffin oil), mineral waxes, hydrocarbons (advantageously squalane or squalene), synthetic or semisynthetic triglyceride oils (e.g. triglycerides of capric or caprylic acid), natural oils (e.g. apricot kernel oil, avocado oil, cottonseed oil, borage seed oil, thistle oil, groundnut oil, gamma-oryzanol, rosehip seed oil, hemp oil, hazelnut oil, blackcurrant seed oil, coconut oil, cherry kernel oil, salmon oil, flax oil, maize oil, macadamia nut oil, almond oil, evening primrose oil, mink oil, olive oil, palm oil, pecan nut oil, peach kernel oil, pistachio nut oil, rapeseed oil, rice bran oil, castor oil, safflower oil, sesame oil, soya oil, sunflower oil, teatree oil, grape seed oil or wheat germ oil, and the like), natural ester oils (e.g. jojoba oil), synthetic ester oils (preferably esters of saturated and/or unsaturated, linear and/or branched alkane carboxylic acids having 3 to 30 C atoms with saturated and/or unsaturated, linear and/or branched alcohols having 3 to 30 C atoms and esters of aromatic carboxylic acids with saturated and/or unsaturated, linear and/or branched alcohols having 3 to 30 C atoms, selected in particular from the group comprising isopropyl myristate, isopropyl stearate, isopropyl palmitate, isopropyl oleate, n-butyl stearate, n-hexyl laurate, n-decyl laurate, isooctyl stearate, isononyl stearate, isononyl isononanoate, 2-ethylhexyl palmitate, 2-ethylhexyl laurate, 2-ethylhexyl ethylhexanoate, cetearyl-2-ethylhexanoate, 2-hexyldecyl stearate, 2-octyldecyl palmitate, oleyl oleate, oleyl erucate, erucyl oleate, erucyl erucate and synthetic or natural blends of such esters), fats, waxes and other natural and synthetic fat bodies, preferably esters of fatty alcohols with low C-number alcohols (e.g. with isopropanol, propylene glycol or glycerol) or esters of fatty alcohols with low C-number alkanoic acids or with fatty acids,

alkyl benzoates (e.g. mixtures of n-dodecyl, n-tridecyl, n-tetradecyl and n-pentadecyl benzoate) and cyclic or linear silicone oils (such as e.g. dimethyl polysiloxanes, diethyl polysiloxanes, diphenyl polysiloxanes and mixed forms thereof).

The aqueous phase of formulations according to the invention (in particular topical cosmetic formulations) optionally advantageously contains low C-number alcohols, diols or polyols, and ethers thereof, preferably ethanol, isopropanol, propylene glycol, glycerol, ethylene glycol, ethylene glycol monoethyl or monobutyl ether, propylene glycol monomethyl ether, monoethyl or monobutyl ether, diethylene glycol monomethyl or monoethyl ether and analogous products, also low C-number alcohols, e.g. ethanol, isopropanol, 1,2-propanediol, glycerol, also α- or β-hydroxy acids, preferably lactic acid, citric acid or salicylic acid, as well as emulsifiers, which can advantageously be selected from the group of ionic, non-ionic, polymeric, phosphate-containing and zwitterionic emulsifiers, and in particular one or more thickeners, which can advantageously be selected from the group comprising silicon dioxide, aluminium silicates, such as e.g. bentonites, polysaccharides or derivatives thereof, e.g. hyaluronic acid, guar gum, xanthan gum, hydroxypropyl methyl cellulose or allulose derivatives, particularly advantageously from the group comprising polyacrylates, preferably a polyacrylate from the group of so-called carbopols, in each case either individually or in combination or from the group of polyurethanes.

The formulations according to the invention (e.g. topical cosmetic formulation) advantageously contain cooling agents. Examples of cooling agents which can be cited are: l-menthol, menthone glycerol acetal, menthyl lactate, substituted menthyl-3-carboxylic acid amides (e.g. menthyl-3-carboxylic acid-N-ethylamide), 2-isopropyl-N-2,3-trimethyl butanamide, substituted cyclohexane carboxylic acid amides, 3-menthoxypropane-1,2-diol, 2-hydroxyethyl menthyl carbonate, 2-hydroxypropyl menthyl carbonate, N-acetyl glycine menthyl ester, menthyl hydroxycarboxylic acid esters (e.g. menthyl-3-hydroxybutyrate), monomenthyl succinate, 2-mercaptocyclodecanone, menthyl-2-pyrrolidin-5-one carboxylate.

The formulations according to the invention (e.g. topical cosmetic formulations) also advantageously contain antimicrobial active ingredients. Examples which can be cited are:

Aryl- or aryloxy-substituted, unbranched or monoalkyl- and polyalkyl-branched saturated or mono- to pentaunsaturated (up to five double or triple bonds, also mixed ene/ine compounds) fatty alcohols, fatty aldehydes and fatty acids having chain lengths of C_2 to C_{40}.

Aryl- or aryloxy-substituted, unbranched or monoalkyl- and polyalkyl-branched saturated or mono- to pentaunsaturated (up to five double or triple bonds, also mixed ene/ine compounds) alkane diols, dialdehydes and dicarboxylic acids having chain lengths of C_2 to C_{40}, particularly preferably chain lengths of C_4 to C_{12}.

Mono- and oligoglycerides (up to 4 glycerol units) of aryl- or aryloxy-substituted unbranched or monoalkyl- and polyalkyl-branched saturated or mono- to pentaunsaturated (up to five double or triple bonds, also mixed ene/ine compounds) fatty alcohols (mono- and oligoglycerol monoalkyl ethers), fatty acids (mono- and oligoglycerol monoalkyl esters), alkanediols (mono- and oligoglycerol monoalkyl ethers; bis(mono-/oligoglyceryl)alkyl diethers) and dicarboxylic acids (mono- and oligoglycerol monoalkyl esters; bis(mono-/oligoglyceryl) alkyl diesters) having chain lengths of C_2 to C_{40}.

Fatty acid esters of unbranched or monoalkyl- and polyalkyl-branched saturated or mono- to pentaunsaturated (up to five double or triple bonds, also mixed ene/ine compounds), optionally also aryl- or aryloxy-substituted, carboxylic acids having chain lengths of C_2 to C_{40} with unbranched or monoalkyl- and polyalkyl-branched saturated or mono- to pentaunsaturated (up to five double or triple bonds, also mixed ene/ine compounds), optionally also aryl- or aryloxy-substituted, monohydric to hexahydric fatty alcohols having chain lengths of C_2 to C_{40}.

Plant and animal fatty acid cuts, containing unbranched or monoalkyl- and polyalkyl-branched saturated or mono- to pentaunsaturated (up to five double or triple bonds, also mixed ene/ine compounds) fatty alcohols, fatty aldehydes

and fatty acids having chain lengths of C_2 to C_{40} (e.g. coconut fatty acids, palm kernel fatty acids, wool wax acids).

Mono- and oligoglycerides of lanolin, of lanolin alcohols and lanolic acids (e.g. glyceryl lanolate, neocerite), glycyrrhetic acid and derivatives (e.g. glycyrrhetinyl stearate), natural and synthetic cardenolides (e.g. digitoxin, dogoxin, digoxygenin, gitoxygenin, strophanthin and strophanthidin), natural and synthetic bufadienolides (e.g. scillaren A, scillarenin and bufotalin), sapogenins and steroid sapogenins (e.g. amyrins, oleanolic acid, digitonin, gitogenin, tigogenin and diosgenin), steroid alkaloids of plant and animal origin (e.g. tomatidin, solanin, solanidin, conessin, batrachotoxin and homobatrachotoxin).

Mono- and polyhalogenated nitriles, dinitriles, trinitriles or tetranitriles.

Mono- and oligohydroxy fatty acids having chain lengths of C_2 to C_{24} (e.g. lactic acid, 2-hydroxypalmitic acid), oligomers and/or polymers thereof and plant and animal raw materials containing these.

Acyclic terpenes: terpene hydrocarbons (e.g. ocimene, myrcene), terpene alcohols (e.g. geraniol, linalool, citronellol), terpene aldehydes and ketones (e.g. citral, pseudoionone, ß-ionone); monocyclic terpenes: terpene hydrocarbons (e.g. terpinene, terpinolene, limonene), terpene alcohols (e.g. terpineol, thymol, menthol), terpene ketones (e.g. pulegone, carvone); bicyclic terpenes: terpene hydrocarbons (e.g. carane, pinane, bornane), terpene alcohols (e.g. borneol, isoborneol), terpene ketones (e.g. camphor); sesquiterpenes: acyclic sesquiterpenes (e.g. farnesol, nerolidol), monocyclic sesquiterpenes (e.g. bisabolol), bicyclic sesquiterpenes (e.g. cadinene, selinene, vetivazulene, guajazulene), tricyclic sesquiterpenes (e.g. santalene), diterpenes (e.g. phytol), tricyclic diterpenes (e.g. abietic acid), triterpenes (squalenoids; e.g. squalene), tetraterpenes.

Ethoxylated, propoxylated or mixed ethoxylated/propoxylated cosmetic fatty alcohols, fatty acids and fatty acid esters having chain lengths of C_2 to C_{40} with 1 to 150 E/O and/or P/O units.

Antimicrobial peptides and proteins having an amino acid value from 4 to 200, e.g. Skin Antimicrobial Peptides (SAPs), Lingual Antimicrobial Peptides (LAPs), human ß-defensins (in particular h-BD1 and h-BD2), lactoferrins and hydrolysates thereof and peptides obtained therefrom, Bactericidal/Permeability Increasing Proteins [BPIs], Cationic Microbial Proteins [CAPs], lysozyme.

Very suitable carbohydrates or "carbohydrate derivatives", which in the interests of brevity can also be included under the term "carbohydrates", are compounds containing sugars and substituted sugars or sugar groups. The sugars include in particular also the deoxy and dideoxy forms, N-acetyl galactosamine-, N-acetyl glucosamine- and sialic acid-substituted derivatives as well as sugar esters and ethers. Preference is given to

a) monosaccharides, including in particular pentoses and hexoses,

b) disaccharides, including in particular sucrose, maltose, lactobiose,

c) oligosaccharides, including in particular the tri- and tetrasaccharides, and

d) polysaccharides, including in particular starch, glycogen, cellulose, dextran, tunicin, inulin, chitin, in particular chitosans, chitin hydrolysates, alginic acid and alginates, plant gums, body mucosa, pectins, mannans, galactans, xylans, araban, polyoses, chondroitin sulfates, heparin, hyaluronic acid and glycosaminoglycanes, hemicelluloses, substituted cellulose and substituted starch, in particular the hydroxyalkyl-substituted polysaccharides in each case.

Amylose, amylopectin, xanthan, α-, β- and γ-dextrin are particularly suitable. The polysaccharides can consist of e.g. 4 to 1,000,000, in particular 10 to 100,000, monosaccharides. Chain lengths are preferably chosen in each case which ensure that the active ingredient is soluble in or can be incorporated into the particular preparation.

Sphingolipids such as sphingosine; N-monoalkylated sphingosines; N,N-dialkylated sphingosines; sphingosine-1-phosphate; sphingosine-1-sulfate; psychosine (sphingosine-ß-D-galactopyranoside); sphingosyl phosphoryl cholin; lysosulfatides (sphingosyl galactosyl sulfate; lysocerebroside sulfate); lecithin; sphingomyelin; sphinganine.

So-called "natural" antibacterial active ingredients can also be used, most of which are essential oils. Typical oils having an antibacterial action are, for example, oils of aniseed, lemon, orange, rosemary, wintergreen, clove, thyme, lavender, hops, citronella, wheat, lemongrass, cedarwood, cinnamon, geranium, sandalwood, violet, eucalyptus, peppermint, gum benzoin, basil, fennel, menthol and Ocmea origanum, Hydastis carradensis, Berberidaceae daceae, Ratanhiae or Curcuma longa.

Important substances having an antimicrobial action which can be found in essential oils are for example anethol, catechol, camphene, carvacrol, eugenol, eucalyptol, ferulic acid, farnesol, hinokitiol, tropolone, limonene, menthol, methyl salicylate, thymol, terpineol, verbenone, berberine, curcumin, caryophyllene oxide, nerolodol, geraniol.

Mixtures of the cited active systems or active ingredients and active ingredient combinations containing these active ingredients can also be used.

The amount of active ingredients in the preparations is preferably 0.01 to 20 wt.%, based on the total weight of the preparations, particularly preferably 0.05 to 10 wt.%.

The formulations according to the invention (in particular cosmetic, including dermatological formulations) can contain deodorants, i.e. active ingredients having a deodorising and perspiration-inhibiting action. These include, for example, odour maskers, such as the common perfume constituents, antiperspirants based on aluminium, zirconium or zinc salts, odour absorbers, for example the layered silicates described in the laid-open patent specification DE-P 40 09 347, in particular montmorillonite, kaolinite, nontronite, saponite, hectorite, bentonite, smectite, and also zinc salts of ricinoleic acid, for example. They also include deodorants, bactericidal or

bacteriostatic deodorising substances, such as e.g. hexachlorophene, 2,4,4'-trichloro-2'-hydroxydiphenyl ether (Irgasan), 1,6-di-(4-chlorophenylbiguanido)hexane (chlorhexidine), 3,4,4'-trichlorocarbanilide, and the active agents described in the laid-open patent specifications DE-37 40 186, DE-39 38 140, DE-42 04 321, DE-42 29 707, DE-42 29 737, DE-42 37 081, DE-43 09 372, DE-43 24 219 and containing cation-active substances, such as e.g. quaternary ammonium salts and odour absorbers such as e.g. Grillocin® (combination of zinc ricinoleate and various additives) or triethyl citrate, optionally in combination with ion-exchange resins.

The amount of deodorising and/or antiperspirant active ingredients in the formulations is preferably 0.01 to 20 wt.%, based on the total weight of the preparations, particularly preferably 0.05 to 10 wt.%.

Formulations according to the invention can also contain preservatives. On the one hand, all antioxidants which are suitable or commonly used for cosmetic and/or dermatological applications can be used as preservatives.

Traditional preservatives (e.g. formaldehyde, glutardialdehyde, parabens (e.g. methyl, ethyl, propyl and butyl paraben), dibromodicyanobutane, imidazolidinyl ureas ("Germall"), isothiazolinones ("Kathon"), methyl chlorothiazolidine, methyl thiazolidine, organic acids (e.g. benzoic acid, sorbic acid, salicylic acid) and salts and esters thereof, propionic acid and formic acid and salts thereof, glycols (e.g. propylene glycol, 1,2-dihydroxyalkanes), plant-based preservative aids and flavonoids (e.g. lantadin A, caryophyllene, hesperidin, diosmin, phellandrene, pigenin, quercetin, hypericin, aucubin, diosgenin, plumbagin, corlilagin, etc.) and glycosylated derivatives thereof (e.g. glycosyl rutin)

Formulations according to the invention, in particular dermatological formulations, can also advantageously contain dyes and/or coloured pigments, particularly if they are intended for use in the area of decorative cosmetics. The dyes and coloured pigments can be selected from the corresponding positive list in the German cosmetics ordinance or the EU list of cosmetic colorants. In most cases they are identical to the dyes approved for foodstuffs. Advantageous coloured pigments are for example titanium dioxide, mica, iron oxides (e.g. Fe_2O_3 Fe_3O_4, FeO(OH)) and/or tin oxide. Advantageous dyes are

for example carmine, Berlin blue, chromium oxide green, ultramarine blue and/or manganese violet.

If the dermatological formulations according to the invention are intended for use in the facial area, it is convenient to choose as the dye one or more substances from the following group: 2,4-dihydroxyazobenzol, 1-(2'-chloro-4'-nitro-1'-phenylazo)-2-hydroxynaphthalene, Ceres red, 2-(4-sulfo-1-naphthylazo)-1-naphthol-4-sulfonic acid, calcium salt of 2-hydroxy-1,2'-azonaphthalene-1'-sulfonic acid, calcium and barium salts of 1-(2-sulfo-4-methyl-1-phenylazo)-2-naphthyl carboxylic acid, calcium salt of 1-(2-sulfo-1-naphthylazo)-2-hydroxynaphthalene-3-carboxylic acid, aluminium salt of 1-(4-sulfo-1-phenylazo)-2-naphthol-6-sulfonic acid, aluminium salt of 1-(4-sulfo-1-naphthylazo)-2-naphthol-3,6-disulfonic acid, 1-(4-sulfo-1-naphthylazo)-2-naphthol-6,8-disulfonic acid, aluminium salt of 4-(4-sulfo-1-phenylazo)-1-(4-sulfophenyl)-5-hydroxypyrazolone-3-carboxylic acid, aluminium and zirconium salts of 4,5-dibromofluorescein, aluminium and zirconium salts of 2,4,5,7-tetrabromofluorescein, 3',4',5',6'-tetrachloro-2,4,5,7-tetrabromofluorescein and its aluminium salt, aluminium salt of 2,4,5,7-tetraiodofluorescein, aluminium salt of quinophthalone disulfonic acid, aluminium salt of indigo disulfonic acid, red and black iron oxide (CIN: 77491 (red) and 77499 (black)), iron oxide hydrate (CIN: 77492), manganese ammonium diphosphate and titanium dioxide.

Also advantageous are oil-soluble natural dyes, such as e.g. paprika extracts, β-carotene or cochineal.

Also advantageous within the meaning of the present invention are dermatological formulations containing pearlescent pigments. The types of pearlescent pigment listed below are particularly preferred:

1. Natural pearlescent pigments, such as e.g.

- "pearl essence" (guanine/hypoxanthine mixed crystals obtained from fish scales) and

- "mother of pearl" (ground mussel shells)

2. Monocrystalline pearlescent pigments such as e.g. bismuth oxychloride (BiOCl)

3. Layered substrate pigments: e.g. mica / metal oxide

The basis for pearlescent pigments is formed for example by powdered pigments or castor oil dispersions of bismuth oxychloride and/or titanium dioxide and bismuth oxychloride and/or titanium dioxide on mica. The lustre pigment listed under CIN 77163 is particularly advantageous, for example.

The list of cited pearlescent pigments is naturally not intended to be limiting. Advantageous pearlescent pigments within the meaning of the present invention are obtainable in many ways known per se. For example, substrates other than mica can be coated with other metal oxides, such as e.g. silica and the like. SiO_2 particles coated with TiO_2 and Fe_2O_3 ("Ronaspheres"), for example, which are sold by Merck and are particularly suitable for the optical reduction of fine lines, are advantageous.

It can also be advantageous to dispense altogether with a substrate such as mica. Iron pearlescent pigments, which are produced without the use of mica, are particularly preferred. Such pigments are available from BASF, for example, under the trade name Sicopearl Copper 1000.

Particularly advantageous also are special effect pigments, which are available from Flora Tech under the trade name Metasomes Standard / Glitter in various colours (yellow, red, green, blue). Here the glitter particles are mixed with various auxiliary substances and dyes (for example the dyes with the colour index (CI) numbers 19140, 77007, 77289, 77491).

The dyes and pigments can be present both singly and mixed together and coated with one another, wherein different colour effects can generally be obtained by means of varying coating thicknesses. The total amount of dyes and colouring pigments is advantageously chosen from the range from e.g. 0.1 wt.% to 30 wt.%, preferably 0.5 to 15 wt.%, in particular 1.0 to 10 wt.%, based in each case on the total weight of the cosmetic formulations.

Mixtures of the cited active systems can also be used.

The amount of active ingredients in the formulations according to the invention is preferably 0.01 to 20 wt.%, based on the total weight of the formulation, particularly preferably 0.05 to 10 wt.%.

For use, topical formulations according to the invention, in particular formulations for skin and hair lightening, are applied to the skin and/or hair in an adequate amount in the conventional manner for cosmetics.

Other preferred embodiments of the invention can be seen from the following examples and the appended claims:

Example 1: "Oil-in-water" emulsion

Part	Raw material name (manufacturer)	Chemical name	Content in wt.%
A	Arlatone 983 S® (ICI)	PEG-5 glyceryl stearate	1.2
	Brij 76® (ICI)	Steareth-10	1.2
	Cutina MD® (Cognis)	Glyceryl stearate	3.5
	Baysilone oil M10® (GE Bayer)	Dimethicone	0.8
	Eutanol G® (Cognis)	Octyl dodecanol	3.0
	Paraffin oil 65 cp (Henry Lamotte)	Mineral oil	8.0
B	Water, dist.	Aqua (water)	49.6
	Phenopip® (Nipa Laboratorien)	Phenoxyethanol (and) methylparaben (and) ethylparaben (and) butylparaben (and) propylparaben (and) isobutylparaben	0.5
	Trilon BD® (BASF)	Disodium EDTA	0.1
	1,2-Propylene glycol	Propylene glycol	2.0
	Glycerol 99 %	Glycerol	3.0
	Salicin		0.2
C	Water, dist.	Aqua (water)	25.0
	Carbopol 2050® (B.F. Goodrich)	Carbomer	0.4
	Aqueous sodium hydroxide sol., 10%	Sodium hydroxide	1.2
D	Perfume oil	Parfum (fragrance)	0.3

Part A was mixed and heated to 80°C. Part B was mixed and heated to 90°C and added to part A whilst stirring. For part C, Carbopol was carefully dispersed in water and neutralised with sodium hydroxide solution (pH 6.9). Part C was then added to the mixture of parts A and B at 60°C. Part D was added to the mixture of parts A, B and C at room temperature.

Example 2: "Water-in-oil" emulsion with UVA/B broad-band protection

Part	Raw material name (manufacturer)	Chemical name	Content in wt.%
A	Dehymuls PGPH® (Cognis)	Polyglycerol-2 dipolyhydroxystearate	3.0
	Monomuls 90-O 18® (Cognis)	Glyceryl oleate	1.0
	Permulgin 2550® (Koster Keunen Holland)	Beeswax	1.0
	Myritol 318® (Cognis)	Caprylic/capric acid triglycerides	6.0
	Witconol TN® (Witco)	C_{12}-C_{15} alkyl benzoate	6.0
	Cetiol SN® (Cognis)	Cetyl and stearyl isononanoate	5.0
	Copherol 1250® (Cognis)	Tocopherol acetate	1.0
	Solbrol P® (Bayer)	Propylparaben	0.1
	Neo Heliopan® AV (Symrise)	Ethylhexyl methoxycinnamate	4.0
	Neo Heliopan® E 1000 (Symrise)	Isoamyl-p-methoxycinnamate	4.0
	Neo Heliopan® MBC (Symrise)	4-Methylbenzylidene camphor	2.0
	Neo Heliopan® OS (Symrise)	Ethylhexyl salicylate	3.0
	Octyl triazone	Ethylhexyl triazone	1.0
	Zinc oxide neutral (Symrise)	Zinc oxide	7.0
B	Water, dist.	Aqua (water)	39.5
	Trilon BD® (BASF)	Disodium EDTA	0.1
	Phenoxyethanol		0.7
	Solbrol M (Bayer)	Methylparaben	0.2
	Glycerol 99 %		4.0
	Neo Heliopan® AP (Symrise), 15 % as sodium salt	Disodium phenyl dibenzimidazole tetrasulfonate	10.0
	Benzophenone-4	Benzophenone-4	0.5
	Salicin		0.5
C	Perfume oil	Perfume	0.3
	Bisabolol	Bisabolol	0.1

For part A all substances apart from the zinc oxide were heated to 85°C and the zinc oxide was carefully dispersed in the mixture. The components of part B were mixed together, heated to 85°C and added to part A whilst stirring. Part C was added to the mixture of parts A and B and the mixture was then homogenised with a dispersing tool.

Example 3: "Oil-in-water" emulsion with UVA/B broad-band protection

Part	Raw material name (manufacturer)	Chemical name	Content in wt.%
A	Arlacel 165® (ICI)	Glyceryl stearate and polyethylene glycol 100-stearate	3.0
	Emulgin B2® (Cognis)	Ceteareth-20	1.0
	Lanette O® (Cognis)	Cetyl and stearyl alcohol	1.15
	Myritol 318® (Cognis)	Caprylic/capric acid triglycerides	5.0
	Cetiol SN® (Cognis)	Cetyl and stearyl isononanoate	4.0
	Abil 100® (Goldschmidt)	Dimethicone	1.0
	Bentone Gel MIO® (Rheox)	Mineral oil and quaternium-18-hectorite and propylene carbonate	3.0
	Cutina CBS® (Cognis)	Glyceryl stearate and cetyl alcohol and stearyl alcohol and cetyl palmitate and cocoglyceride	2.0
	Neo Heliopan® 303 (Symrise)	Octocrylene	7.0
	Neo Heliopan® BB (Symrise)	Benzophenone-3	1.0
	Neo Heliopan® MA (Symrise)	Menthyl anthranilate	3.0
	N,N-Dimethyl-4-aminobenzoic acid-2-ethylhexyl ester		3.0
	Titanium dioxide, microfine	Titanium dioxide	5.0
B	Water, dist.		53.85
	Trilon BD® (BASF)	Disodium EDTA	0.1
	Veegum ultra® (Vanderbilt)	Magnesium aluminium sulfate	1.0
	Natrosol 250 HHR (Aqualon)	Hydroxymethylcellulose	0.3
	Glycerol	Glycerol	3.0
	Phenopip® (Nipa Laboratorien)	Phenoxyethanol (and) methylparaben (and) ethylparaben (and) butylparaben (and) propylparaben (and) isobutylparaben	0.3
	Salicin		2.0
C	Perfume oil		0.3

For part A, all substances apart from the titanium dioxide were mixed together and heated to 85°C; the titanium dioxide was carefully dispersed into the mixture. For part B all substances apart from the Veegum and Natrosol were mixed together, heated to 90°C, the Natrosol and Veegum dispersed into the mixture and the mixture added to part A whilst stirring. Part C was added to the mixture of parts A and B and the mixture was then homogenised with a dispersing tool.

Example 4: "Oil-in-water" emulsion with UVA/B broad-band protection

Part	Raw material name (manufacturer)	Chemical name	Content in wt.%
A	Emulsiphos (Symrise)	Cetyl phosphate, hydrogenated palm glyceride	1.50
	Cutina MD® (Cognis)	Gyceryl stearate	2.0
	Lanette 16® (Cognis)	Cetyl alcohol	1.2
	Neutral oil (Symrise)	Caprylic/capric acid triglycerides	5.0
	Cetiol SN® (Cognis)	Cetyl isononanoate	5.0
	Copherol 1250® (Cognis)	Tocopherol acetate	0.5
	Solbrol P® (Bayer)	Propylparaben	0.1
	Abil 100® (Goldschmidt)	Dimethicone	0.3
	Trilon BD® (BASF)	Disodium EDTA	0.1
	Neo Heliopan® HMS (Symrise)	Homosalate	5.0
	Neo Heliopan® 357 (Symrise)	Butyl methoxy dibenzoylmethane	2.0
B	Water, dist.		47.1
	1,3-Butylene glycol		3.0
	Sobrol M® (Bayer)	Methylparaben	0.2
	Phenoxyethanol		0.7
	Carbopol ETD 2050® (B.F. Goodrich)	Carbomer	0.2
	Keltrol T® (Calgon)	Xanthan gum	0.2
	Neo Heliopan® AP (Symrise)	Disodium phenyl dibenzimidazole tetrasulfonate	22
	Kojic acid	Kojic acid	0.5
	Salicin		0.2
C	Aqueous sodium hydroxide sol., 10%	Sodium hydroxide	2.8
D	Perfume oil	Perfume oil	0.3
	Bisabolol	Bisabolol	0.1

Part A was heated to 85°C. Carbopol and Keltrol were dispersed cold into the remaining constituents, the mixture heated to 85°C and added to part A. Part C was immediately added to the mixture of parts A and B at 80°C and homogenised with a dispersing tool for 5 min. Finally part D was added at room temperature and the mixture homogenised with a dispersing tool.

Example 5: "Oil-in-water" emulsion with UVA/B broad-band protection

Part	Raw material name (manufacturer)	Chemical name	Content in wt.%
A	Hostacerin DGMS® (Clariant)	Polglyceryl-2-stearate	3.0
	Lanette 16® (Cognis)	Cetyl alcohol	2.0
	Prisorine 3505® (UniQema)	Isostearic acid	0.5
	Tegosoft TN® (Goldschmidt)	C_{12}-C_{15} alkyl benzoate	2.0
	Copherol 1250® (Cognis)	Tocopherol acetate	0.5
	Neutral oil (Symrise)	Caprylic/capric acid triglyceride	5.0
	Solbrol P® (Bayer)	Propylparaben	0.1
	SF1214® (Bayer)	Cyclopentasiloxane, dimethicone	1.0
	Corapan TQ® (Symrise)	Diethylhexyl-1,6-naphthalate	3.0
	Neo Heliopan® HMS (Symrise)	Homosalate	9.5
	Neo Heliopan® 357 (Symrise)	Butyl methoxy dibenzoylmethane	0.6
	Keltrol T® (Kelco)	Xanthan gum	0.2
B	Water, dist.	Aqua (water)	49.25
	Lanette E (Cognis)	Sodium cetearyl sulfate	0.75
	Glycerol 99 %	Glycerol	4.0
	Phenoxyethanol (Symrise)	Phenoxyethanol	0.7
	Edeta BD® (BASF)	Disodium EDTA	0.1
	Neo Heliopan® Hydro (15 % aqueous solution neutralised with NaOH) (Symrise)	Phenylbenzimidazole sulfonic acid	6.7
	Neo Heliopan® AP (10 % aqueous solution neutralised with NaOH) (Symrise)	Disodium phenyl dibenzimidazole tetrasulfonate	10.0
	Salicin		0.2
	Solbrol M®(Bayer)	Methylparaben	0.2
C	Symrise perfume oil (Symrise)	Perfume oil	0.5
	NaOH 10% aqueous solution	Sodium hydroxide	0.2

Part A was heated to 80°C. After dissolving all constituents, the mixture was heated to 85°C, Keltrol added and the mixture stirred for 5 min. The mixture was then homogenised for 10 min with a dispersing tool. The mixture was heated to 85°C, part B added, the mixture stirred for 10 min at 80°C and then

homogenised at 60°C. Finally part C was added at room temperature and the mixture homogenised with a dispersing tool.

Example 6: Oil-free sun spray with UVA/B broad-band protection

Part	Raw material name (manufacturer)	Chemical name	Content in wt.%
A	Water, dist.		22.2
	Glycerol 99 %	Glycerol	4.5
	Neo Heliopan® Hydro (15 % aqueous solution neutralised with NaOH) (Symrise)	Phenylbenzimidazole sulfonic acid	33.3
	Neo Heliopan® AP (10 % aqueous solution neutralised with NaOH) (Symrise)	Disodium phenyl dibenzimidazole tetrasulfonate	22.0
	Salicin		0.2
	D-Pantheol (BASF)	Panthenol	0.5
	Keltrol T® (Kelco)	Xanthan gum	0.2
	Euxyl K 100® (Schülke & Mayr)	Benzyl alcohol, methyl chloroisothiazolinone, methyl isothiazolinone	0.1
	Dow Corning® 193 (Dow Corning)	Dimethicone copolyol	1.0
	Extrapone Aloe Vera (Symrise)		1.0
	Extrapone Camomile (Symrise)		1.0
	Extrapone Witch Hazel (Symrise)		1.0
B	Ethanol (96%)	Ethyl alcohol	13.0

Mix together all ingredients for part A apart from Keltrol. Add Keltrol whilst stirring, and continue stirring until the mixture is homogeneous. Add part B and stir until homogeneous.

Example 7. Skin-lightening balm with UVA/UVB protection

Part	Raw material name (manufacturer)	INCI name	% (w/w)
A	Demineralised water	Water (aqua)	51.70
	Hydrolite (Symrise)	Pentanediol	4.30
	Carbopol ETD 2001 (Noveon)	Carbomer	0.50
	Salicin		**1.0**
	Keltrol T (Kelco)	Xanthan gum	0.30
B	Neo Heliopan® Hydro (15 % aqueous solution neutralised with NaOH) (Symrise)	Phenylbenzimidazole sulfonic acid	10.00
	Sodium hydroxide solution, 10% aq.	Sodium hydroxide	2.20
C	Neo Heliopan® AV (Symrise)	Ethylhexyl methoxycinnamate	5.00
	Neo Heliopan® E 1000 (Symrise)	Isoamyl p-methoxycinnamate	5.00
	Neo Heliopan® MBC (Symrise)	4-Methylbenzylidene camphor	2.00
	Neo Heliopan® 357 (Symrise)	Butyl methoxy dibenzoylmethane	1.50
	Alpha-Bisabolol (Symrise)	Bisabolol	0.10
	Baysilone Oil PK 20 (GE Bayer)	Phenyl trimethicone	5.00
	Tegosoft TN (Degussa)	C12-15 Alkyl benzoate	4.00
	Unimer U-151 (Induchem)	PVP/hexadecene copolymer	0.50
	Copherol 1250 (Cognis)	Tocopheryl acetate	0.50
	Edeta BD (BASF)	Disodium EDTA	0.10
D	Ethyl alcohol (96 vol.%), denatured	SD alcohol 39-C	5.00
	Symrise perfume oil	Fragrance (perfume)	0.30
	Phenoxyethanol (Symrise)	Phenoxyethanol	0.70
	Solbrol M (Bayer)	Methylparaben	0.20
	Solbrol P (Bayer)	Propylparaben	0.10

Mix together all raw materials for part A apart from Keltrol and Carbopol. Carefully add Keltrol and Carbopol whilst stirring vigorously. Mix together all raw materials for part B and add to part A whilst stirring. Mix together all raw materials for part C thoroughly and heat gently until Neo Heliopan® 357 is dissolved. Then add part C to part A/B and stir until homogeneous. For part D, dissolve Solbrol P and M in the other raw materials and then add slowly to part A/B/C. Stir until the product is homogeneous and homogenise. The pH of the end product should be between 7.2 and 7.5.

Production of the 15% Neo Heliopan® Hydro solution:

82.85% water, demineralised

02.15% sodium hydroxide, 99%

15.00% Neo Heliopan® Hydro PN 103089

Dissolve two-thirds of the sodium hydroxide in water, then add Neo Heliopan® Hydro whilst stirring. Add the remaining sodium hydroxide until the solution becomes clear. The pH of the final Neo Heliopan® Hydro solution should be 7.5 to 8.0. The addition of preservatives is recommended for extended storage periods.

Example 8: Skin-lightening aerosol foam with UVB/UVA protection

Part	Raw material name (manufacturer)	INCI name	% (w/w)
A	Emulsiphos (Symrise)	Cetyl phosphate, hydrogenated palm glycerides	1.50
	Cutina MD (Cognis)	Glyceryl stearate	2.00
	Lanette 16 (Cognis)	Cetyl alcohol	0.50
	Texapon N 70 (Cognis)	Sodium laureth sulfate	0.10
	Neutral oil (Symrise)	Caprylic/capric triglyceride	2.00
	Tegosoft TN (Degussa)	C12-15 Alkyl benzoate	2.00
	Copherol 1250 (Cognis)	Tocopheryl acetate	0.50
	Solbrol P (Bayer)	Propylparaben	0.10
	Edeta BD (BASF)	Disodium EDTA	0.10
	Neo Heliopan® AV (Symrise)	Ethylhexyl methoxycinnamate	6.00
	Neo Heliopan® MBC (Symrise)	4-Methylbenzylidene camphor	4.00
	Neo Heliopan® 357 (Symrise)	Butyl methoxy dibenzoylmethane	1.50
B	Demineralised water	Water (aqua)	58.30
	Salicin		0.50
	Glycerol 99 %	Glycerol	3.00
	Solbrol M (Bayer)	Methylparaben	0.20
	Phenoxyethanol (Symrise)	Phenoxyethanol	0.70
	Carbopol ETD 2050 (Noveon)	Carbomer	0.10
C	Sodium hydroxide 10% aq.	Sodium hydroxide	2.90
	Neo Heliopan® Hydro (15 % aqueous solution neutralised with NaOH) (Symrise)	Phenylbenzimidazole sulfonic acid	13.30
D	Symrise perfume oil	Fragrance (perfume)	0.40
	Alpha-Bisabolol (Symrise)	Bisabolol	0.10

Heat part A to 85°C. For part B disperse Carbopol evenly in water, then add all other raw materials for part B and heat to 85°C. Add part B to part A whilst stirring. Add part C directly to part A/B and leave to cool. Add part D to part A/B/C and introduce into aerosol containers. The pH of the end product should be around 7.5.

Example 9: Skin-lightening non-aerosol foam

Part	Raw material name (manufacturer)	INCI name	% (w/w)
A	Demineralised water	Water (aqua)	70.50
	Glycerol 99 %	Glycerol	4.00
	Hydrolite5 (Symrise)	1,2-Pentylene glycol	5.00
	D-Panthenol (BASF)	Panthenol	0.50
	Salicin		**0.20**
	Lara Care A-200 (Rahn)	Galactoarabinan	0.25
	Texapon N 70 (Cognis)	Sodium laureth sulfate	0.50
B	Baysilone Oil M 10 (Bayer)	Dimethicone	1.00
	Edeta BD	Disodium EDTA	0.10
	Copherol 1250 (Cognis)	Tocopheryl acetate	0.50
	Neo Heliopan® MBC (Symrise)	4-Methylbenzylidene camphor	3.00
	Neo Heliopan® AV (Symrise)	Ethylhexyl methoxycinnamate	2.00
	Neo Heliopan® E 1000 (Symrise)	Isoamyl p-methoxycinnamate	6.00
	Neo Heliopan® 357 (Symrise)	Butyl methoxy dibenzoylmethane	1.50
	Alpha-Bisabolol nat. (Symrise)	Bisabolol	0.10
	Symrise perfume oil	Fragrance (perfume)	0.20
	Pemulen TR 2 (Novion)	Acrylates/C10-30 alkyl acrylate crosspolymer	0.25
	Cetiol OE (Cognis)	Dicaprylyl ether	3.00
C	Phenoxyethanol (Symrise)	Phenoxyethanol	**0.70**
	Solbrol M (Bayer)	Methylparaben	0.20
	Solbrol P (Bayer)	Propylparaben	0.10
D	Sodium hydroxide 10% aq.	Sodium hydroxide	0.60

Dissolve all raw materials for part A in water. For part B, dissolve Neo Heliopan® MBC and Neo Heliopan® 357 in Neo Heliopan® AV and E 1000 whilst heating. Add all other constituents of part B at room temperature.

Disperse Pemulen evenly whilst stirring vigorously. Add part B to part A and homogenise. For part C, dissolve Solbrol M and P in phenoxyethanol whilst heating to approx. 50°C and add to part A/B. Add part D to part A/B/C whilst stirring and homogenise. The pH of the end product should be 7.0.

Example 10: Shampoo with skin-lightening properties

Part	Raw material name (manufacturer)	INCI name	% (w/w)
A	Crinipan® AD (Symrise)	Climbazole	0.50
	Dragocide Liquid (Symrise)	Phenoxyethanol (and) methylparaben (and) ethylparaben (and) butylparaben (and) propylparaben (and) isobutylparaben	0.70
B	Texapon NSO BZ (Cognis)	Sodium laureth sulfate	27.00
	Dehyton K	Cocamidopropyl betaine	12.00
	Softigen 767	PEG-6 caprylic/capric glycerides	2.50
	Neo Heliopan® Hydro (15 % aqueous solution neutralised with NaOH) (Symrise)	Phenylbenzimidazole sulfonic acid	3.38
	Arlypon F	Laureth-2	2.00
	Witch Hazel Distillate (Symrise)	Hamamelis virginiana (witch hazel) distillate	1.00
	Alpha Bisabolol, natural (Symrise)	Bisabolol	0.10
	Symrise perfume oil	Fragrance (perfume)	0.50
	D-Panthenol	Panthenol	0.40
C	Demineralised water	Water (aqua)	47.82
	Salicin		**0.2**
	Polymer JR 400	Polyquaternium-10	0.40
D	Solubilizer (Symrise)	PEG 40 hydrogenated castor oil, trideceth-9, propylene glycol, water	3.0
	Neo Heliopan 357 (Symrise)	Butyl methoxy dibenzoylmethane	0.5

Add Crinipan® AD to Dragocide Liquid whilst stirring, until Crinipan® AD is completely dissolved. Mix all constituents of part B with part A whilst stirring until part A/B is homogeneous. Add polymer (part C) to water whilst stirring and stir until completely dissolved. Then add to part A/B. For part D, dissolve the oil components in the solubiliser and add to part A/B/C whilst stirring. The pH of the final anti-dandruff shampoo should be around 7.5.

Example 11: Skin-lightening hair conditioner with UVB/UVA protection

Part	Raw material name (manufacturer)	INCI name	% (w/w)
A	Lanette O (Cognis)	Cetearyl alcohol	2.50
	Eumulgin B 2 (Cognis)	Ceteareth-20	0.70
	Neo Heliopan 357	Butyl methoxy dibenzoylmethane	0.50
	Neo Heliopan® E 1000 (Symrise)	Isoamyl p-methoxycinnamate	2.00
B	Demineralised water	Water (aqua)	91.57
	Crotein Q (Croda)	Hydroxypropyltrimonium hydrolysed collagen	1.00
	Dehyquart SP	Quaternium-52	0.50
	Salicin		**0.20**
	Citric acid	Citric acid	0.13
	Symrise perfume oil	Fragrance (perfume)	0.40
C	Phenonip (Clariant)	Phenoxyethanol (and) methylparaben (and) ethylparaben (and) butylparaben (and) propylparaben (and) isobutylparaben	0.50

Heat part A to 70°C. Dissolve the raw materials for part B apart from the perfume oil in water, heat to 90°C and add this solution to part A whilst stirring. Allow the emulsion to cool to 40°C, stirring slowly, and add the perfume oil whilst stirring. After storing for 24 hours, add the Phenopip whilst stirring. The pH of the end product should be around 3.5.

Example 12: Skin-lightening moisture cream O/W

Part	Raw material name (manufacturer)	Chemical name	Content in wt.%
A	PCL liquid (Symrise)	Cetearyl ethylhexanoate, isopropyl myristate	3.0
	Dragophos S (Symrise)	Sodium dihydroxycetyl phosphate	2.0
	Isodragol (Symrise)	Triisononanoin	7.0
	Dracorin GMS (Symrise)	GLYCERYL STEARATE	2.0
	Lanette 18 (Care Chemicals)	Stearyl alcohol	4.5
	Dow Corning 200 Fluid (Dow Corning)	Dimethicone	2.0
B	Water	Water (aqua)	71.0
	Hydrolite-5 (Symrise)	Pentylene glycol	3.0
	Salicin		1.0
	Mg ascorbyl phosphate	Magnesium ascorbylphosphate	3.0
	Dragocid Liquid (Symrise)	Methylparaben, phenoxyethanol, ethylparaben, butylparaben, propylparaben, isobutylparaben	0.8
	Citric acid 10% solution	Citric acid	0.35
C	Perfume oil	Fragrance	0.35

Swell Carbopol in water. Heat phases A and B separately to 80°C. Add phase B to phase A, and only then emulsify. Cold-stir with a paddle agitator. Reduce the stirring speed as the temperature falls. At 40°C add the raw materials for phase C.

Example 13: Skin-lightening face cream O/W

Part	Raw material name (manufacturer)	Chemical name	Content in wt.%
A	Dracorin 100 s.e. P (Symrise)	Glyceryl stearate, PEG-100 stearate	8.0
	Dracorin GMS (Symrise)	Glyceryl stearate	3.0
	Paraffin oil 5 grade E (Parafluid)	Paraffinum liquidum	4.0
	Lanette 16 (Care Chemicals)	Cetyl alcohol	2.0
	Isopropyl myristate (Symrise)	Isopropyl myristate	8.0
	Abil 350 (Goldschmidt)	Dimethicone	0.3
B	Water	Water (aqua)	67.85
	Propylene glycol-1,2 99 P GC (Dow Benelux)	Propylene glycol	5.0
	Salicin		0.5
	Neo-Dragocid powder (Symrise)	Methylparaben, sorbic acid, dehydroacetic acid, propylparaben	0.8
	Sodium hydroxide 10% solution	Sodium hydroxide	0.25
	Perfume oil	Fragrance	0.30

Preparation instructions:

Heat phase A and B separately to approx. 80°C. Add phase B to phase A in an Ultra-Turrax agitator and emulsify. Cold-stir the cream with a paddle agitator, reducing the stirring speed from 250 rpm as the temperature falls. Add phase C at approx. 40°C.

Experiment 1 (depigmenting effect)

B16V mouse melanoma cells are disseminated in a 96-well microtitre plate in a concentration of 5 x 10^3 cells/well. After cultivation for 24 h at 37°C and 5% CO_2 in RPMI medium, enriched with 10% foetal calf serum, various concentrations of the test substances and 0.3 mM tyrosine and 10 nM α-MSH (α-melanocyte stimulating hormone) are added and incubated for a further 96 h. The maximum concentration of the test substances used corresponds to 0.1 times the value of the IC_{20} value of the cytotoxicity assay. In parallel the cells are incubated with kojic acid as a control in concentrations of 0.01 mM, 0.1 mM and 1 mM. After incubation, SDS and NaOH (final concentrations: 1 mM and 1 M respectively) are added to the culture medium and the absorption (A) is measured after 3 h at 400 nm.

The inhibition of pigmentation in the presence of the test compounds or kojic acid was calculated using the following equation:

Inhibition of pigmentation (%) = 100- [($A_{test\ compound}/A_{control}$) x 100]

From the inhibition of pigmentation (%) in a series of dilutions of test compounds, the IC_{50} for each test compound is calculated. This is the concentration of a test compound at which pigmentation is inhibited by 50%.

Table 3

Test substance	**IC_{50} (µM)**
Kojic acid	452.3
2-(Hydroxymethyl)-phenyl-ß-D-glucopyranoside (salicin)	164.3
2-(Hydroxymethyl) benzyl alcohol (saligenin)	210.9
2-Hydroxy-3-methoxy benzyl alcohol	inactive

This data shows that salicin and saligenin have an approximately 3 times stronger depigmenting effect on B16V melanoma cells than kojic acid. An additional methoxy substitution of the phenyl ring in the 3 position leads to a loss of depigmenting activity.